An unusual case involving a uterine serous carcinoma with an intercurrent lymphatic PEComa

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Abstract Perivascular epithelioid cell tumors (PEComas) are comprised of an assortment of epithelioid cells with a varying perivascular distribution. We document the history of a patient who originally presented with a stage I uterine serous carcinoma. However, upon further pathologic review, an incidental PEComa was fortuitously identified in one of her pelvic lymph nodes. The finding of a PEComa in conjunction with primary uterine cancer is extremely rare; consequently, gynecologic oncologists should consider precluding a metastatic process prior to determining optimal patient management.

Keywords Perivascular epithelial neoplasms · Lymph node · Uterine carcinoma · Gynecologic oncology

Introduction

Perivascular epithelioid cell tumors (PEComas) are soft tissue neoplasms with a distinct, perivascular distribution [1]. This lesion is comprised of discrete subtypes, namely angiomyolipoma, lymphangiomyoma and clear-cell pulmonary neoplasms [2]. Occasionally, PEComas coincide with the tuberous sclerosis complex, a condition characterized by mental retardation, seizures and cellular proliferation [3].

Perivascular epithelioid cell tumors, albeit incompletely defined, represent a subtype of uterine epithelioid mesenchymal tumors [4]. PEComas exhibit an array of spindle and epithelioid shapes, clear to granular cytoplasm, and a perivascular location; they are also consistently immunoreactive to the melanocytic marker HMB45, variably immune-reactive to smooth muscle actin and negative for epithelial markers [4, 5].

Perivascular epithelioid cell tumors with limited, precarious attributes (e.g., pleomorphism) may coincide with benign behavior or an uncertain malignant potential. Conversely, when the neoplasm has multiple, high risk histologic features, the disease should be considered malignant [6]; classification, however, of the disease's histogenesis and propensity for malignancy is imprecise.

The manifestation of a PEComa originating from the gynecologic tract is very rare [3, 7]; when this condition occurs, the uterine corpus is the most common location. Nevertheless, the detection of a PEComa within a pelvic lymph node, even an incidental occurrence, coinciding with a synchronous uterine serous carcinoma is extremely unusual.

Case report

A 69-year-old (gravid 2, para 2) woman presented with presumed multiple fibroids on pelvic ultrasound (Fig. 1). A subsequent endometrial biopsy was negative and thereafter, she underwent a hysteroscopy and D&C performed by her gynecologist; final pathology revealed uterine serous carcinoma in the endometrial curettings. The patient was referred for gynecologic oncology consultation forthwith. Her medical history was significant for a cholecystectomy, glaucoma, hypertension, mitral valve prolapse, diabetes, thrombophlebitis and hypothyroidism.

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Fig. 1 Pelvic ultrasound exhibits a 1.6×1.6 cm right, anterior fibroid. Also, a 1.4×1.3 cm posterior lower uterine segment fibroid is noted; two additional sub-centimeter fibroids are visualized

The patient underwent a robotic-assisted hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymphadenectomy, right para-aortic lymphadenectomy and omental biopsy. During the laparoscopy, the uterus, ovaries, fallopian tubes and upper abdomen appeared normal. A right para-aortic lymphadenectomy was conducted; however, the left para-aortic region could not be adequately visualized due to multiple loops of small intestine, and thus an ipsilateral lymphadenectomy was contra-indicated. All of the sampled lymph nodes and omentum appeared grossly negative for metastatic disease. Hemostasis was excellent with an estimated blood loss of 50 ml; there were no evident intra-operative complications.

Pathologic evaluation precluded any residual serous carcinoma in the uterus (i.e., there was no evidence of lymph-vascular space invasion, myometrial invasion or cervical involvement); furthermore, the surgical margins were negative for invasive carcinoma (Fig. 2a–c). There were six left pelvic lymph nodes submitted for review; in accordance with immunohistochemical staining (e.g., MELAN-A, HMB45, and H&E), one node contained a histologically benign PEComa (Fig. 3a–d). A subsequent CT scan of the chest, abdomen, and pelvis did not reveal additional sites of PEComa (or metastatic serous endometrial carcinoma); the patient has since done well with 6 months of follow-up.

Discussion

Perivascular epithelioid cell tumors are very rare lesions that differ in presentation and have a variable description. The neoplasm was initially described in 1992; thence, less than 75 cases have been reported with only select reports that involved the uterus [8–12] (see Table 1).

Fig. 2 **a** High grade serous carcinoma of the endometrium, H&E stain, original magnification ($\times 200$). **b** High grade serous carcinoma of the endometrium, H&E stain, original magnification ($\times 400$). **c** High grade serous carcinoma of the endometrium, P53 Immunostain, original magnification ($\times 200$); the glands in the lower part of the field are uninvolved and p53 negative

Perivascular epithelioid cell tumors are predominantly benign but can present with high mitotic activity, necrosis and nuclear atypia [1, 5, 13]. The PEComa in the present case was a peculiar finding insofar as the lesion, albeit

Fig. 3 **a** PEComa involving lymph node capsule, H&E stain, original magnification ($\times 40$). **b** PEComa involving lymph node capsule, H&E stain, original magnification ($\times 400$). **c** PEComa involving lymph node capsule, HMB45 immunohistochemical stain (*brown chromogen*),

original magnification ($\times 100$). **d** PEComa involving lymph node capsule, MELAN-A immunohistochemical stain (*red chromogen*), original magnification ($\times 100$)

Table 1 Select reported cases involving PEComas with uterine involvement

Reference	Age	Site	Histopathology	Immuno-histochemistry	Outcome
Dimmler et al. [11]	61	Uterus	Infiltrative LVSI low to intermediate nuclear grade ^a	HMB45 and SMA positive; desmin negative	NED at 9 months ^b
Park et al. [12]	32	Uterus	Infiltrative; epithelioid intermediate nuclear grade; necrosis; 1 MF/50 HPF	HMB45 & CD117 positive; SMA, desmin, S100-protein negative	NED at 18 months
Greene et al. [8]	79	Uterus	Infiltrative; epithelioid intermediate to high Nuclear grade; necrosis; 8 MF/10 HPF	HMB45, Melan-A, SMA & S100 protein-positive; desmin, ER/PR-negative	Pelvic recurrence at 24 months; patient expired several months later
Fink et al. [9]	51	Broad ligament	Highly cellular; partially necrotic; Pleomorphic with spindled and epithelioid features	HMB45 & Melan-A positive; SMA, desmin & S100 protein positive	NED at 15 months
Fadare [13]	41	Uterine cervix	Infiltrative; mixed epithelioid/spindled; low to intermediate grade with cellularity; <1 MF/50 HPF	HMB45 & Melan-A positive; SMA, desmin & S100 protein positive	NED at 35 months

^a LVSI-lympho-vascular space invasion

^b NED-no evidence of disease

benign, coincided with the patient's uterine serous carcinoma.

Following a review of the literature, only a few studies documenting endometrial carcinoma with a coexistent PEComa were reported [14, 15]; specifically, Iwasa et al. [15] reported on three uterine cancer patients who were also diagnosed with an incidental extra-pulmonary lymphangioliomyoma (LAM) in the pelvic and para-aortic lymph nodes. All of them underwent hysterectomy and bilateral salpingo-oophorectomy with a pelvic and para-aortic lymphadenectomy. One could speculate that there is a relationship between LAM and uterine cancer; in the Hayashi et al. [14] study, they reported that 90 % of their subjects with pulmonary LAM also had uterine lesions.

Perivascular epithelioid cell tumors are neoplasms of undefined histogenesis and malignant potential that appear to exhibit select morphologic and immunophenotypic overlap with smooth muscle neoplasia [13]. Moreover, they apparently comprise a subset of HMB-45-positive epithelioid mesenchymal tumors of the uterus although their specific relationship with pure smooth muscle tumors is indeterminate [4].

Perivascular epithelioid cell tumors of soft tissue and gynecologic provenance may be classified as malignant or of uncertain malignant potential. However, in the absence of disquieting clinical features (e.g., larger lesions, lymphovascular space or myometrial invasion) as discussed in the current study, PEComas are predominantly benign [6]. Initially, we were concerned that the PEComa in the current study represented a metastatic process. However, further imaging studies precluded any additional sites of PEComa; thus, the disease's provenance remains indeterminate. We recognize that since CD10 and CD1a also demonstrate immunopositivity, additional immunohistochemistry studies may have further contributed to the identification of the PEComa's origination [16]; had there been any evidence of a metastatic PEComa, vincristine, ifosfamide and doxorubicin chemotherapy would have been considered as an adjunct to surgery [13].

Despite the rare incidence, a coexistent lesion in the lymphatic system should be considered when gynecologic oncologists are performing a staging procedure on any patient with a gynecologic neoplasm. The implications from the present case study suggest that further histological evaluation of the PEComa is necessary to facilitate accurate diagnosis and potentially improve upon clinical management.

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Conflict of interest The authors declare that they have no conflict of interest.

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